

## GUEST COMMENTARY

### *qnr* Gene Nomenclature<sup>∇</sup>

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Since the plasmid-borne quinolone resistance gene *qnr* was reported in 1998 (8), many additional *qnr* alleles have been discovered on plasmids or the bacterial chromosome (reviewed in references 9 and 13). The plasmid-borne *qnr* genes currently comprise three families, *qnrA*, *qnrB*, and *qnrS*, differing from each other 40% or more in nucleotide sequence. Within each family, minor ( $\leq 10\%$ ) variation in sequence has defined a growing number of alleles. For the *qnrA* and *qnrS* families, the number of variants has been manageable, with general agreement on allele designations, but lately, the number of *qnrB* sequences submitted to GenBank has exploded, with the same *qnrB* allele number claimed for dissimilar sequences by different investigators and the same entry given new allele numbers from week to week.

To bring order into the current *qnrB* numbering chaos, we propose numbering the *qnr* alleles according to the following rules: (i) priority should be given first to published numbers, then to those in accepted or submitted manuscripts, and finally to the date of submission to GenBank; (ii) only full-length sequences should be assigned allele numbers; (iii) naturally occurring alleles, not those created by mutation, will be numbered; (iv) only nucleotide alterations that result in amino acid changes and not functionally silent substitutions should be taken into account; (v) one or more amino acid alterations define a new allele; (vi) variation in promoter sequences is not considered; (vii) demonstration that an allele in an established family causes reduced susceptibility to nalidixic acid or a fluoroquinolone is desirable but is not required; (viii) a new family (such as *qnrC*) should differ substantially from existing families ( $\geq 30\%$  difference suggested in nucleotides or derived amino acids) and should be shown to affect quinolone susceptibility; (ix) a database of *qnr* allele designations will be maintained at <http://www.lahey.org/qnrStudies>; and (x) further allele numbers will be assigned upon application.

Another source of confusion is the presence of two potential in-frame initiation codons for some *qnrB* alleles. For other *qnrB* alleles, the first ATG is out of phase with the second. The

TABLE 1. Proposed Qnr allele designations

Allele	GenBank accession number		GenBank designation <sup>a</sup>	Reference or source
	Nucleotide	Protein		
QnrA1	AY070235	AAL60061		17
QnrA2	AY675584	AAT79355		T. Li et al., unpublished
QnrA3	DQ058661	AAZ04782		11
QnrA4 <sup>b</sup>	DQ058662	AAZ04783		11
QnrA5 <sup>b</sup>	DQ058663	AAZ04784		11
QnrA6	DQ151889	AAZ78355		2
QnrB1	DQ351241	ABC86904		6
QnrB2	DQ351242	ABC86905		6
QnrB3	DQ303920	ABC17629		14
QnrB4	DQ303921	ABC17630		14
QnrB5	DQ303919	ABC17628		4
QnrB6	EF520349	ABP87778		X. Ma et al., unpublished
QnrB7	EU043311	ABW03156		3
QnrB8	EU043312	ABW03157		3
QnrB9	EF526508	ABP88094	QnrB8	M. Zhu et al., unpublished
QnrB10	DQ631414	ABG56269		12
QnrB11	EF653270	ABS30107	QnrB9	P. Rodriguez-Zulueta et al., unpublished
QnrB12	AM774474	CAO82104		7
QnrB13	EU273755	ABX72042	QnrB12	M. D. Tamang et al., unpublished
QnrB14	EU273757	ABX72044		M. D. Tamang et al., unpublished
QnrB15	EU302865	ABX72227		M. D. Tamang et al., unpublished
QnrB16	EU136183	ABV66096	QnrB11	J. Sanchez-Cespedes et al., unpublished
QnrB17	AM919398	CAP45902	QnrB16	J. Gonzalez-Lopez et al., unpublished
QnrB18	AM919399	CAP45903	QnrB17	J. Gonzalez-Lopez et al., unpublished
QnrB19	EU432277	ACA28712		V. Cattoir et al., unpublished
QnrS1	AB187515	BAD88776		5
QnrS2	DQ485530	ABF47470		4
QnrS3	EU077611	ABU52984		L. Yue et al., unpublished

<sup>a</sup> Number currently in GenBank if different from that assigned.

<sup>b</sup> Known only in the chromosome of *Shewanella algae*.

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TABLE 2. Amino acid substitutions in QnrA1 to QnrA6

Allele	Substitution at position:							
	39	54	108	116	127	130	161	213
QnrA1	Q	V	V	S	T	S	R	V
QnrA2	R			A	A			I
QnrA3	R		I		A			
QnrA4	R		I		A	N		
QnrA5	R		I		A		C	
QnrA6	R	I	I		A		H	

second ATG initiation codon, common to all, has been used here in numbering QnrB amino acids, and amino acid variations that would occur if the first initiation codon were used have been ignored. Consequently, QnrB proteins have 214 amino acids, whereas the QnrA and QnrS proteins are 218 amino acids in length.

*qnr* alleles in the GenBank database as of April 2008 were evaluated to identify unique sequences and then assigned allele numbers. Table 1 shows our proposed designations for *qnrA*, *qnrB*, and *qnrS*. No new full-length *qnrA* sequences were found, but a unique *qnrS* sequence was identified and designated *qnrS3*. Nineteen unique *qnrB* alleles were identified. GenBank listings for partial *qnrB* alleles (accession numbers EF421178, EF421180, EF571009, EF576718, EU127476, and EU325573) have been omitted. In addition, GenBank accession numbers EF634464 and EU093091 code for QnrB6, and accession number EU136182 encodes QnrB9. Accession number EU273765, expressed from the second potential start codon, is the same as QnrB13 in our listing. Tables 2, 3, and 4 show the amino acid alterations in particular variants. Although *qnrB* has the greatest number of sequence variants, amino acid differences are currently found at 27 of 214 possible sites (13%), a percentage less than the amino acid variability among TEM (20%) or SHV (27%) β-lactamases (<http://www.lahey.org/Studies/>).

*qnr* genes have also been found on the chromosomes of both gram-positive (15) and gram-negative bacteria. We propose that they be termed *qnr* from a particular organism or, where a shorter designation is needed, given distinguishing initials such as *Efsqnr* from *Enterococcus faecalis* (1), *Ppqnr* from *Photobacterium profundum* (10), *Vpqr* from *Vibrio parahaemolyticus* (16), or *Vvqr* from *Vibrio vulnificus* (10). *qnr* letter designations, such as *qnrA3* from *Shewanella algae* or *SaqnrA3* should be used only if the gene is at least 70% identical to one of the established *qnr* families.

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TABLE 3. Amino acid substitutions in QnrB1 to QnrB19<sup>a</sup>

Allele	Amino acid change at position:																														
	2	11	18	20	21	22	55	60	69	79	80	89	94	129	142	144	151	162	163	168	171	186	188	198	202	204	205	212	213		
QnrB1	A	D	E	I	E	N	N	M	S	A	S	A	A	V	I	A	F	S	T	A	F	I	G	N	S	L	M	V	I		
QnrB2															M																
QnrB3							K								M																
QnrB4	T			V				N	I	V	N	S			M				S				S	S		L		I	M		
QnrB5	T			V					V	V					M																
QnrB6															M																
QnrB7															M																
QnrB8								I	V	V	A				M				S	T					A						
QnrB9									V	V	A				M																
QnrB10	T			V					V	V					M																
QnrB11	T		A	V				I	V	V		S			M																
QnrB12	T		A	V				I	V	V		S			M																
QnrB13									V	V					M																
QnrB14					D				A	A	N				M																
QnrB15						S			A	A					M																
QnrB16									A	A					M																
QnrB17									A	A					M																
QnrB18					D				A	A					M																
QnrB19	T			V					V	V					M									S							

<sup>a</sup> Variations from the QnrB1 sequence numbered from the second potential ATG initiation codon are shown.

TABLE 4. Amino acid substitutions in QnrS1 to QnrS3

Allele	Amino acid substitution at position:																	
	5	11	12	16	21	31	41	44	89	91	102	106	120	148	201	206	207	216
QnrS1	N	H	N	K	L	S	T	V	F	A	T	H	S	N	A	L	I	Y
QnrS2	R		S	Q	I	C	A	I	L	E	A	N	T	H	S	Q	L	F
QnrS3		R																

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